



## Clinical trial results:

**An Open-Label, Pilot Study to assess the effect of Lanadelumab on the clinical signs and symptoms of Hereditary angioedema with normal C1-inhibitor // LANC (Lanadelumab in Hereditary Angioedema with normal C1-esterase inhibitor)**

### Summary

EudraCT number	2018-004136-30
Trial protocol	DE
Global end of trial date	03 July 2024

### Results information

Result version number	v1 (current)
This version publication date	15 January 2026
First version publication date	15 January 2026

### Trial information

#### Trial identification

Sponsor protocol code	DEALSZ-2018-001
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
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Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 July 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 July 2024
Global end of trial reached?	Yes
Global end of trial date	03 July 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To assess the effect of Lanadelumab on the clinical signs and symptoms in patients with HAE-nC1.

Protection of trial subjects:

The study was conducted in accordance with the ICH E6 (R2) Guideline for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, German Medicinal Products Act (AMG)), and with the ethical principles that have their origins in the Declaration of Helsinki (version 2013). The Investigator also had to comply with all applicable privacy regulations (e.g., Regulation (EU) 2016/679 (General Data Protection Regulation, GDPR)).

Background therapy:

Hereditary angioedema (HAE) is a rare genetic disease with an estimated prevalence in the general population of approximately 1:50.000. The disease is characterized by localized and self-limiting swelling of the subcutaneous and/or submucosal tissue without wheals or other signs of urticaria due to a temporary increase in vascular permeability caused by the release of vaso-active mediators. The clinical expression is highly variable, from asymptomatic cases to patients with disabling and life-threatening attacks, and it has a

demonstrated humanistic and economic burden. Swelling attacks in patients with Hereditary Angioedema with normal C1 inhibitor (HAE-nC1INH) are caused by activation of the contact system and the subsequent generation of bradykinin, which causes extravasation by activating the bradykinin-B2 receptor. This pathomechanism is thought to also be involved in some types of HAE-nC1INH. Lanadelumab (Takhzyro, Takeda Pharmaceutical Company Limited) was approved in the United States in October 2018 by the Food and Drug Administration (FDA) and in November 2018 in Europe by the European Medicine Agency (EMA), for long-term prophylaxis in HAE in patients 12 years or older, with a later approval extending the indication to children aged 2 years and older.

At the time this study was planned, there was only few data available on the efficacy and safety of Lanadelumab in patients with HAE-nC1INH. Therefore, the aim of this Phase 2, exploratory, proof-of concept, single-center, single-arm, open-label pilot interventional study was to assess the effects and safety of Lanadelumab in patients with HAE-nC1INH.

Evidence for comparator: -

Actual start date of recruitment	24 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

5 patient with clinical symptoms of angioedema attacks (at least 2 attacks within the last 3 months prior to screening; and at least 2 attacks within 12 weeks at maximum in the run-in period) and documented HAE-nC1INH (history, a FXII / PLG / ANGPT1 / KNG1 / MYOF / HSST mutation ...) were enrolled and received treatment at one study site.

### Pre-assignment

Screening details:

The study consisted of a screening period of 4 to 12 weeks. 7 eligible patients were screened. 1 patients did not meet all eligibility criteria at Screening and 1 patient declined to participate.

### Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

this study was planned and conducted as a proof-of-concept, open-label, singlearm trial.

### Arms

Arm title	Treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lanadelumab
Investigational medicinal product code	CAS Number 1426055-14-2
Other name	Takzhyro
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients received an injection of 300 mg Lanadelumab every 2 weeks.

Lanadelumab is a human monoclonal antibody (class IgG1 kappa) that targets plasma kallikrein (pKal) in order to promote prevention of angioedema in people with hereditary angioedema.

Before enrollment, patients were required to discontinue certain medications that could interfere with the investigational medicinal product or study endpoints, with a defined washout period implemented as needed. It was required that patients, at the time of enrollment, were not enrolled in another investigational treatment or device study and did not take any investigational agent for 4 weeks or 5 half-lives, whichever is longer, since the end of another investigational device or drug trial. The use of rescue medication was monitored and reviewed throughout the treatment period and if necessary, adjusted. The use of rescue medication was also part of the efficacy assessment.

Number of subjects in period 1	Treatment
Started	5
Completed	4
Not completed	1
Adverse event, non-fatal	1



## Baseline characteristics

### Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	5	5	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	1	1	

## End points

### End points reporting groups

Reporting group title	Treatment
Reporting group description: -	

### Primary: change of Angioedema Activity Score (AAS)

End point title	change of Angioedema Activity Score (AAS) <sup>[1]</sup>
End point description: AAS28 ≥75% responders	
End point type	Primary
End point timeframe: At week 48 compared to the AAS at week 0 (baseline).	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to the limited patient numbers of with Hereditary Angioedema with normal C1-esterase inhibitor, the sample size (n=5-7) is not based on statistical methodology but reflects the number of available patients at the center.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	4 <sup>[2]</sup>			
Units: score				
median (standard deviation)				
weeks 9-12	25.89 (± 46.11)			
weeks 21-24	24.72 (± 48.10)			
weeks 33-36	37.91 (± 46.43)			
weeks 45-48	15.27 (± 74.62)			

Notes:

[2] - after week 33 only 3 subjects were analysed, because of lost to follow up

<b>Attachments (see zip file)</b>	tables and charts _primary -secondary endpoints/DEALZ-2018-
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### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

overall study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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### Reporting groups

Reporting group title	Treatment
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Reporting group description: -

Serious adverse events	Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Hereditary angioedema attack			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Varicose vein			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %



Non-serious adverse events	Treatment		
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 5 (100.00%)		
Injury, poisoning and procedural complications postoperative pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2		
Contusion subjects affected / exposed occurrences (all)	Additional description: lower leg, shoulder region, wrist 1 / 5 (20.00%) 3		
Nervous system disorders Hypertension subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 5		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)  Dental caries subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1  1 / 5 (20.00%) 1		
Psychiatric disorders Loss of libido subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Renal and urinary disorders renal insufficiency subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2		

Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
COVID-19 infection, mild subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Pharyngitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2019	update protocol version 2.0, <ul style="list-style-type: none"><li>• Correction of Sample size calculation</li><li>• "Investigator's Brochure" replaced by "Specialist Information"</li><li>• Information on approval status of Lanadelumab added</li><li>• correction of study outline</li><li>• interim analysis removed</li><li>• Early study termination section specified</li><li>• Change in person Serious Adverse events must be reported to</li><li>• Addition of success criterion</li></ul>
20 December 2019	update protocol version 3.0 <ul style="list-style-type: none"><li>• Anti-drug antibody assessment deleted from synopsis</li><li>• Addition of newly found KNG1 mutation to table 1</li><li>• information on approval status of Lanadelumab was adjusted,</li><li>• Primary endpoint, secondary endpoints, statistical analyses and sample size calculation were adjusted</li><li>• Details for labelling of IMP were added</li><li>• Specification of early study termination criteria</li><li>• Adverse Event not used as abbreviations anymore to avoid confusion with Angioedema</li><li>• Adverse event reporting added at all timepoints in schedule of assessments</li><li>• Explanation of AAS and AE-QoL questionnaire expanded</li></ul>
28 February 2020	update protocol version 3.1: <ul style="list-style-type: none"><li>• Success criterion added for 6 or 7 patients</li><li>• Sample size calculation amended for power analysis</li></ul>
22 October 2021	update protocol version 4.0: <ul style="list-style-type: none"><li>• CentoCard® included for blood biomarkers</li><li>• Bilirubin to laboratory added</li><li>• Specification of MedDRA Version 22.0</li></ul>
19 April 2023	update protocol version 5.0: <ul style="list-style-type: none"><li>• Deletion of CentoCard® for blood biomarkers</li><li>• Adjustment of applicable legislation (no reference to US law)</li><li>• Three recently discovered mutations (KNG1, MYOF, HSST) added as inclusion criterion</li><li>• Update of Database Management and Quality Control (section 10.4) as well as Data Analysis (section 11) – paper CRF and SPSS will be used</li><li>• Adjustment of study termination criteria</li></ul>
06 July 2023	update protocol version 6.0: <ul style="list-style-type: none"><li>• Adjustment of study termination criteria</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the limited patient numbers of with Hereditary Angioedema with normal C1-esterase inhibitor, the sample size (n=5-7) is not based on statistical methodology but reflects the number of available patients at the center.

Notes: